# PSJ17 Exh 54

**DEPARTMENT OF HEALTH & HUMAN SERVICES** Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-747

AnestaCorporation
C/o Cephalon, Inc.
145 Brandywine Pkwy.
West Chester, PA 19380-4245

Attention: Carol S. Marchione
Senior Director, Regulatory Affairs

Dear Ms. Marchione:

Please refer to your New Drug Application (NDA) for Actiq (oral transmucosal fentanyl citrate).

We also refer to your telephone conversation with Dr. Rappaport, Director of this Division, on June 3, 2004, in which he requested that Cephalon meet with the Agency to present all of the available information on certain aspects of the Actiq product. These aspects were to include all information related to pediatric exposure, abuse, diversion, misuse, overdose, death, off-label use, and any and all information that you are aware of related to non-compliance with the risk management program for the product by sales representatives, other company employees, prescribers, dispensers and/or patients.

We are particularly concerned that Actiq be promoted strictly within its approved indication and only to its appropriate target audience. We remind you that, per the *Indications and Usage* section of the Actiq Package Insert, "Actiq is intended to be used only in the care of cancer patients and only by oncologists and pain specialists who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain." As you know, these restrictions are an important part of the Risk Management Program for the drug, to discourage inappropriate and potentially dangerous misuse of the drug. We would like to know how your company targets physicians that are not oncologists for visits by sales representatives promoting Actiq, or for receiving printed promotional messages (e.g., advertisements or mailings) for Actiq, and what steps, if any, your company takes to ensure that these targeted physicians are pain specialists who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain and do indeed routinely treat cancer patients. We also would like to know if you have knowledge of any reported or actual incidents where sales representatives have detailed physicians on Actiq who do not fit within this description and what, if any, steps were taken to address and remedy the situation.

Similarly, the Agency is concerned that all promotional messages for Actiq clearly convey the restrictions on its indication, namely, that Actiq is only indicated for the management of breakthrough **cancer** pain in **opioid-tolerant** patients and is contraindicated in the management of acute or postoperative pain. We would like to know the steps your company takes to ensure that there is no confusion about the appropriate indicated use of this drug. We are aware that your company

disseminates unbranded "disease awareness" materials discussing "breakthrough pain" generally. Please inform us whether these materials are ever used in conjunction with promotion of Actiq (e.g., as part of a detail in which the sales representative also discusses Actiq, or disseminated with printed materials for Actiq), such that the totality could suggest a benefit for Actiq in treating a broader than indicated population of pain patients, and what steps, if any, your company takes to ensure that such off-label promotion does not occur with these materials. Please also detail how your company monitors and ensures that its sales representatives comply with the laws and regulations regarding promotion of Actiq (e.g., the prohibitions on off-label promotion).

The meeting is scheduled for:

Date: Wednesday, July 14, 2004
Time: 1:00 pm EST
Location: Parklawn Conference Center, Potomac Room
5600 Fishers Lane, Rockville, MD 20857
CDER participants:

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| Robert Meyer, M.D. | Director, ODE II |
| Terry Martin | Regulatory Health Project Manager, OEP/EOS |
| Bob Rappaport, M.D. | Division Director, HFD-170 |
| Rigoberto Roca, M.D, | Deputy Division Director, HFD-170 |
| Elizabeth McNeil, M.D. | Medical Officer, HFD-170 |
| Ravi Harapanhalli, Ph.D. | Chemistry Team Leader, HFD-170 |
| Jo Wyeth, R.Ph. | Safety Evaluator, ODS |
| Martin Pollock, R.Ph. | Safety Evaluator, ODS |
| Lanh Green, Pharm. D. | ODS Team Leader |
| Silvia Calderon, Ph.D. | CSS Reviewer |
| Deborah Leiderman, M.D. | Director, CSS |
| Kathy Miracco | Office of Compliance |
| Carol Krueger | Office of Compliance |
| Thomas Abrams, R. Ph., M.B.A. | Director, DDMAC |
| Carol Barstow, J.D. | Special Assistant to the Director, DDMAC |
| Kristin Davis, J.D. | Regulatory Counsel, DDMAC |
| Spencer Salis, Pharm.D. | Group leader, DDMAC |
| Brenda Marques, Pharm.D. | Senior Regulatory Reviewer, DDMAC |
| Parinda Jani | Chief, Project Management Staff, HFD-170 |
| Kim Compton | Regulatory Project Manager, HFD-170 |

Please have all attendees bring photo identification and allow 15-30 minutes to complete security clearance. Please email me a list of attendees at comptonk@cder.fda.gov so that I can give the security staff time to prepare temporary badges in advance. Upon arrival at FDA, give the guards either of the following numbers to request an escort to the conference room: Kim Compton, 301-827-7432 or the Division secretary at 301-827-7410.

Provide the background information for this meeting (three copies to the NDA and 25 desk copies to me) as soon as possible prior to the meeting.

If you have any questions, contact Kimberly Compton at (301) 827-7432.

Sincerely,

*{See appended electronic signature page}*

Thomas W. Abrams, R.Ph., M.B.A.
Director
Division of Drug Marketing,
Advertising and Communication

*{See appended electronic signature page}*

Bob Rappaport, M.D.
Director
Division of Anesthetic, Critical Care,
Addiction Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/
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Bob Rappaport
6/29/04 05:52:55 PM

Thomas Abrams
6/29/04 06:03:03 PM